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10/652,114

08/29/2003

Jay K. Bass

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EXAMINER

FORMAN, BETTY J

ART UNIT

PAPER NUMBER

1634

MAIL DATE

DELIVERY MODE

06/19/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**Office Action Summary**

Application No.

10/652,114

Applicant(s)

BASS ET AL.

Examiner

BJ Forman

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 April 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 30 and 32-49 is/are pending in the application.
- 4a) Of the above claim(s) 40-43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 30, 32-39 and 44-49 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |                                                                                                            |                                                                                         |
|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 16 April 2007 has been entered.

### ***Status of the Claims***

2. This action is in response to papers filed 16 April 2007 in which claims 30 and 44 were amended, claim 31 was canceled. The amendments add the controller of Claim 31 to the apparatus of Claim 30 and further define the controller of Claim 30 and 44 as having a program for controlled movement of the robotic arm mechanism. The amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 18 January 2007 under 35 U.S.C. 112, second paragraph are withdrawn in view of the amendments. The previous rejections under 35 U.S.C. 102(b)/103 and under 35 U.S.C. 103(a) and under obviousness-type double patenting is maintained. Applicant's arguments have been thoroughly reviewed and are discussed below as they apply to the instant rejections. New grounds for rejection are discussed.

Claims 30, 32-39, 44-49 are under prosecution.

### ***Claim Rejections - 35 USC § 102/103***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 30-31, 33 rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Blanchard (WO 98/41531, published 24 September 1998).

Regarding Claim 30, Blanchard discloses an apparatus for biopolymer array synthesis (Fig. 5), the apparatus comprising a plurality of flow cells (page 74, line 32-page 75, 20), the flow cells comprising a chamber (#80, fig. 9) and a holder for the support (plate #70) wherein the support is a flat glass (page 57, lines 5-13) and the array comprises a plurality of biopolymer features in a pattern on the surface (2-d array, page 57, lines 5-7). Blanchard further discloses the apparatus comprising a fluid dispensing station in fluid communication with the flow cells (inlets in communication with solvent containers via valves and tubing, page 66, lines 2-12) a station for monomer addition, (print head assembly #24) and a mechanism for moving a support to and from the monomer addition station and a flow cell (scanning transport, #22 and treating transport #23) wherein the mechanism comprises a robotic arm (computer controlled transport arms, page 74, lines 8-31) and a holding element comprising a grasping element (grooved vacuum chuck, page 61, lines 21-32 and page 66, line 25-page 67, line 8). Blanchard teaches the apparatus comprises a controller for controlled movement of the mechanism (computer controlled transport arms, page 74, lines 8-31). Blanchard further teaches the computer comprises software programs for moving and positioning the support between various components via the transporters (page 69, lines 15-25, page 70, line 28-page

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71 and Fig. 11) and specifically teaches repeatedly moving the substrate between the print head assembly and flow cell (page 71, lines 3-5 and Page 72, line 27-page 73-17).

Regarding Claim 33, Blanchard teaches the apparatus wherein the flow cells comprise inlet and outlet ports (#83 & #84, Fig. 5).

The preceding rejection is based on judicial precedent following *In re Fitzgerald*, 205 USPQ 594 because Blanchard is silent with regard to the transporter moving the support from one flow cell to another. Blanchard specifically teaches a plurality of flow cells (page 74, line 32-page 75, line 20) and specifically teaches repeated computer-controlled movement of the substrate between the print head assembly and flow cell (page 71, lines 3-5 and Page 72, line 27-page 73-17). Hence, Blanchard teaches that the computer-controlled transporters repeatedly position the substrate in one of a plurality of flow cells. Blanchard, however is silent regarding whether the substrate is transported into "another" flow cell.

However, the transporting mechanism recited in Claim 30 is deemed to be inherent in the multi-flow-cell device and transporters for moving supports into and out of the flow cells via computer-controlled transporters (page 71, lines 3-5 and Page 72, line 27-page 73-17). The transporters are programmed to transport the substrate into a flow cell multiple times. The open claim language "comprising" encompasses additional steps e.g. intervening transport of the substrate to the print head assembly. Furthermore, the claim recites "another flow cell", but does not define another flow cell as a different (i.e. physically distinct) flow cell. Because Blanchard teaches the structural requirements and computer-controlled transporter for repeated movement of the substrate into flow cells, Blanchard teaches all the structural elements required by the claim.

Alternatively, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to provide the transporters of Blanchard with a program to move the substrate from one flow cell into different flow cell. Blanchard teaches the method of synthesis in Example 2, which substrate treatments include 19 iterations of:

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- The substrate was **rinsed** with acetonitrile to remove excess reagents,
- dried with anhydrous nitrogen.
- The resulting substrate was **submerged** in a bath
- The substrate was then rinsed again with acetonitrile,
- The resulting substrate was rinsed with acetonitrile
- dried with anhydrous nitrogen
- then **dipped** for 60 seconds in a solution of 2.5% dichloroacetic acid
- a final rinse with acetonitrile
- a drying stream of dry nitrogen,

And Finally, the substrate was **dipped** in undiluted

The derivatized substrate was affixed to an X-Y translation stage that was driven by two stepping motors via a lead screw. A computer, along with an appropriate electronic interface, was used to synchronize the firing of the inkjet print head with the motion of the X-Y translation stage, so as to deliver one 42 pL drop of the appropriate nucleoside phosphoramidite solution, followed by one 42 pL drop of the 5-ethylthiotetrazole solution to each region of the substrate where oligonucleotide synthesis was to take place. This reaction, which resulted in the coupling of each nucleoside to the substrate via a tetraethyleneglycol linker, was allowed to proceed for 60 seconds under a nitrogen atmosphere. **The substrate was rinsed with acetonitrile to remove excess reagents, and dried with anhydrous nitrogen.**

The resulting substrate was submerged in a bath of the oxidizing solution for 30 seconds so as to convert the resulting nucleoside phosphite triesters to nucleoside phosphate triesters. **The substrate was then rinsed again with acetonitrile,** and then treated with a solution of 20 pL of perfluorooctanoyl chloride in 50 mL of anhydrous xylene, so as to cap all of the unreacted hydroxyl groups of the tetraethylene glycol bonded to the substrate.

The resulting substrate was rinsed with acetonitrile, dried with anhydrous nitrogen, and **then dipped for 60 seconds in a solution of 2.5% dichloroacetic acid in**

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dichloromethane which removed the dimethoxytrityl protecting group from the 5'-hydroxyl group of nucleoside. After a **final rinse with acetonitrile**, and a drying stream of dry nitrogen, the substrate was **subjected to 19 iterations** of the (a) nucleoside coupling, (b) acetonitrile rinsing, (c) oxidation, (d) acetonitrile rinsing, (e) dimethoxytrityl deprotecting and (f) acetonitrile rinsing steps.

Finally, **the substrate was dipped in undiluted** ethanolamine for 20 minutes, at room temperature, to remove both the tBPA protecting groups from the nucleoside bases, and the cyanoethyl groups from the phosphate linkages between adjacent to nucleosides to provide phosphate groups. The substrate was then rinsed with ethanol, and then with acetonitrile, leaving the resulting oligonucleotide attached to the substrate.

Hence, the method of Blanchard consists of rinsing steps with intervening dipping and/or submerging steps. This clearly suggests that the substrates are transported to different flow cells for the (b) acetonitrile rinsing, (c) oxidation, (d) acetonitrile rinsing, (e) dimethoxytrityl deprotecting and (f) acetonitrile rinsing steps. Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was utilize the computer-controlled transporters of Blanchard to transport the support from one flow cell to the next to thereby provide for efficient transport between the vessels for rinsing and dipping and submerging as required in the various synthesis steps recited in Example 2..

#### **Response to Arguments**

6. Applicant asserts that Blanchard does not teach a program for moving the substrate between a monomer addition station and flow cell and between flow cells. The argument has been considered but is not found persuasive because Blanchard specifically teaches a plurality of flow cells (page 74, line 32-page 75, line 20) and specifically teaches repeated computer-programmed movement of the substrate between the print head assembly and flow cell (page 71, lines 3-5 and Page 72, line 27-page 73-17). Hence, Blanchard teaches moving the substrate into one of a plurality of flow cells multiple times. While the claim recites "another

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flow cell”, the claim does not define “another” flow cell as different i.e. physically distinct flow cell. Furthermore, the open claim language “comprising” encompasses additional steps e.g. intervening transport of the substrate to the print head assembly. Therefore, Blanchard teaches the programmed movement as claimed.

Applicant asserts that the Office Action uses hindsight reasoning. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicant asserts that while Blanchard teaches multiple flow cells, Applicant asserts that the multiple flow cells “relates only to multi-tasking, that is, concomitantly synthesizing arrays on the surface of several substrate using a separate flow cell for each substrate.” Applicant's interpretation of the reference is noted, however, Applicant has not pointed to any teaching in the reference of multi-tasking or concomitant synthesis so as to support the assertion. Furthermore, as cited above, Blanchard teaches the synthesis method using various steps of rinsing with intervening steps of dipping and/or submerging (pages 82-85). This clearly suggests that the substrates are transported to different flow cells or fluidic vessel for the various steps of (b) acetonitrile rinsing, (c) oxidation, (d) acetonitrile rinsing, (e) dimethoxytrityl deprotecting and (f) acetonitrile rinsing steps.

***Claim Rejections - 35 USC § 103***

7. Claims 34 and 39 rejected under 35 U.S.C. 103(a) as being unpatentable over Blanchard (WO 98/41531, published 24 September 1998) in view of Goldberg et al (5,959,098, issued 28 September 1999).

Regarding Claims 34 and 39, Blanchard discloses an apparatus for biopolymer array synthesis (Fig. 5), the apparatus comprising a plurality of flow cells (page 74, line 32-page 75, 20), the flow cells comprising a chamber (#80, fig. 9) and a holder for the support (plate #70) wherein the support is a flat glass (page 57, lines 5-13) and the array comprises a plurality of biopolymer features in a pattern on the surface (2-d array, page 57, lines 5-7). Blanchard further discloses the apparatus comprising a fluid dispensing station in fluid communication with the flow cells (inlets in communication with solvent containers via valves and tubing, page 66, lines 2-12) a station for monomer addition, (print head assembly #24) and a mechanism for moving a support to and from the monomer addition station and a flow cell (scanning transport, #22 and treating transport #23) wherein the mechanism comprises a robotic arm (computer controlled transport arms, page 74, lines 8-31) and a holding element comprising a grasping element (grooved vacuum chuck, page 61, lines 21-32 and page 66, line 25-page 67, line 8). Blanchard teaches the claimed fluidic station and monomer addition station in communication with a manifold but is silent regarding a manifold in fluidic communication with the flow cell. However, manifold communication with flow cells for delivery of different reagents for biopolymer synthesis was well known and routinely practiced in the art at the time the claimed invention was made as taught by Goldberg et al (Column 27, lines 12-33). Goldberg teaches that this differential reagent delivery permits batch processing (Column 27, lines 13-15) thereby improves efficiency (Column 24, lines 10-14). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the manifold supplying differential reagent delivery taught by Goldberg to the apparatus of Blanchard. One of ordinary skill in the art would have been motivated to do so for the

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expected benefit of batch processing and efficiency advantages taught by Goldberg (Column 24, lines 10-14).

#### **Response to Argument**

8. Applicant asserts that Goldberg does not cure the deficiencies of Blanchard. The assertion is noted, however as discussed above, Blanchard is not deemed deficient.

9. Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blanchard (WO 98/41531, published 24 September 1998) in view of Hillman et al (U.S. Patent No. 4,856,456, issued 15 August 1989).

Regarding Claim 32, Blanchard discloses an apparatus for biopolymer array synthesis (Fig. 5), wherein the apparatus comprise a holding element comprising a grasping element (grooved vacuum chuck , page 61, lines 21-32 and page 66, line 25-page 67, line 8) but is silent regarding finger-like projections on the vacuum chuck. However, vacuum chucks having finger-like projections were well known in the art of substrate processing as taught by Hillman et al.

Hillman teaches a device for treating a substrate surface wherein the substrate is positioned using a vacuum chuck (#104) having fingers (#152) wherein the fingers enhance the sealing between the substrate and vacuum chuck (Column 9, lines 1-9). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the vacuum chuck of Blanchard by adding the fingers of Hillman. One of ordinary skill in the art would have been motivated to do so for the expected benefit of improved sealing of substrate as taught by Hillman (Column 9, lines 1-9).

#### **Response to Argument**

10. Applicant asserts that Hillman does not cure the deficiencies of Blanchard. The assertion is noted, however as discussed above, Blanchard is not deemed deficient.

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11. Claims 35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blanchard (WO 98/41531, published 24 September 1998) in view of Nokihara (U.S. Patent No. 5,362,447, issued 8 November 1994).

Regarding Claims 35-38, Blanchard discloses an apparatus for biopolymer array synthesis wherein the flow cells have an outlet but does not teach a purification system in communication with the outlet. However, automated synthesizers having column purification systems and sensors attached to flow cell outlets were well known in the art at the time the claimed invention was made as taught by Nokihara.

Nokihara teaches the apparatus wherein expensive and toxic reagents are recycled via a purification column (Column 4, lines 19-27) in communication with a sensor (pH sensor, Column 3, lines 58-67) valve switch (Column 4, lines 28-33) and holding chamber (e.g. fraction collector F, Column 3, lines 1-11). Nokihara teaches the purification system reduces costs by “significantly” reduces the amount of starting material consumed and environmentally destructive waste produced (Column 4, lines 34-44). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the sensor and purification system in the synthesizer of Nokihara to the synthesizer of Blanchard. One of ordinary skill in the art would have been motivated to do so for the expected benefits of reducing costs by “significantly” reducing the amount of starting material consumed and environmentally destructive waste produced (Column 4, lines 34-44).

#### **Response to Argument**

12. Applicant asserts that Nokihara does not cure the deficiencies of Blanchard. The assertion is noted, however as discussed above, Blanchard is not deemed deficient.

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13. Claim 38 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blanchard (WO 98/41531, published 24 September 1998) in view of Kedar (U.S. Patent No. 6,165,778, issued 26 December 2000).

Regarding Claim 38, Blanchard discloses an apparatus for biopolymer array synthesis, wherein the apparatus comprises detecting conditions within the flow cells (Fig. 14 and page 75, lines 1-7) but is silent regarding a sensor in fluid communication with an outlet. However, Kedar teaches an apparatus for array synthesis wherein the apparatus comprises a sensor in fluid communication with the outlet (#111S-119S, Column 74, lines 46-56 and Column 77, lines 35-46) wherein the sensor determines a condition of the reagents (e.g. presence, absence or data) communicates with the controller, which also communicates with the valves.

The claim further recites an intended use for the sensor and controller i.e. that the sensor communicates with a valve to direct fluid reagent to a flow cell or to wastes. However, the recitation of intended use does not further define the structure of the apparatus.

#### **Response to Argument**

14. Applicant asserts that Kedar does not cure the deficiencies of Blanchard. The assertion is noted, however as discussed above, Blanchard is not deemed deficient.

15. Claims 44, 46-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blanchard (WO 98/41531, published 24 September 1998) in view of Goldberg et al (5,959,098, issued 28 September 1999) and Nokihara (U.S. Patent No. 5,362,447, issued 8 November 1994).

Regarding Claims 44, 46-49, Blanchard discloses an apparatus for biopolymer array synthesis (Fig. 5), the apparatus comprising a plurality of flow cells (page 74, line 32-page 75, 20), the flow cells comprising a chamber (#80, fig. 9) and a holder for the support (plate #70) wherein the support is a flat glass (page 57, lines 5-13) and the array comprises a plurality of

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biopolymer features in a pattern on the surface (2-d array, page 57, lines 5-7). Blanchard further discloses the apparatus comprising a fluid dispensing station in fluid communication with the flow cells (inlets in communication with solvent containers via valves and tubing, page 66, lines 2-12) a station for monomer addition, (print head assembly #24) and a mechanism for moving a support to and from the monomer addition station and a flow cell (scanning transport, #22 and treating transport #23) wherein the mechanism comprises a robotic arm (computer controlled transport arms, page 74, lines 8-31) and a holding element comprising a grasping element (grooved vacuum chuck, page 61, lines 21-32 and page 66, line 25-page 67, line 8). Blanchard teaches the apparatus comprises a controller for controlled movement of the mechanism (computer controlled transport arms, page 74, lines 8-31). Blanchard further teaches the computer comprises software programs for moving and positioning the support between various components via the transporters (page 69, lines 15-25, page 70, line 28-page 71 and Fig. 11) and specifically teaches repeatedly moving the substrate between the print head assembly and flow cell (page 71, lines 3-5 and Page 72, line 27-page 73-17).

Furthermore, the claim recites "another flow cell", but does not define another flow cell as a different (i.e. physically distinct) flow cell. Because Blanchard teaches the structural requirements and computer-controlled transporter for repeated movement of the substrate into flow cells, Blanchard teaches all the structural elements required by the claim. Alternatively, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to provide the transporters of Blanchard with a program to move the substrate from one flow cell into different flow cell. Blanchard teaches the method of synthesis in Example 2, which substrate treatments include 19 iterations of rinsing steps with intervening dipping and/or submerging steps. This clearly suggests that the substrates are transported to different flow cells for the (b) acetonitrile rinsing, (c) oxidation, (d) acetonitrile rinsing, (e) dimethoxytrityl deprotecting and (f) acetonitrile rinsing steps. Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was utilize the

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computer-controlled transporters of Blanchard to transport the support from one flow cell to the next to thereby provide for efficient transport between the vessels for rinsing and dipping and submerging as required in the various synthesis steps recited in Example 2.

Blanchard teaches the claimed fluidic station and monomer addition station in communication with a manifold but is silent regarding a manifold in fluidic communication with the flow cell. However, manifold communication with flow cells for delivery of different reagents for biopolymer synthesis was well known and routinely practiced in the art at the time the claimed invention was made as taught by Goldberg et al (Column 27, lines 12-33). Goldberg teaches that this differential reagent delivery permits batch processing (Column 27, lines 13-15) thereby improves efficiency (Column 24, lines 10-14). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the manifold supplying differential reagent delivery taught by Goldberg to the apparatus of Blanchard. One of ordinary skill in the art would have been motivated to do so for the expected benefit of batch processing and efficiency advantages taught by Goldberg (Column 24, lines 10-14). Blanchard and Goldberg do not teach a purification system and sensor in communication with the outlet. However, automated synthesizers having column purification systems and sensors attached to flow cell outlets were well known in the art at the time the claimed invention was made as taught by Nokihara.

Nokihara teaches the apparatus wherein expensive and toxic reagents are recycled via a purification column (Column 4, lines 19-27) in communication with a sensor (pH sensor, Column 3, lines 58-67) valve switch (Column 4, lines 28-33) and holding chamber (e.g. fraction collector F, Column 3, lines 1-11). Nokihara teaches the purification system reduces costs by “significantly” reduces the amount of starting material consumed and environmentally destructive waste produced (Column 4, lines 34-44). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the sensor and purification system in the synthesizer of Nokihara to the synthesizer of Blanchard and/or

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Goldberg. One of ordinary skill in the art would have been motivated to do so for the expected benefits of reducing costs by "significantly" reducing the amount of starting material consumed and environmentally destructive waste produced (Column 4, lines 34-44).

### **Response to Argument**

16. Applicant asserts that Goldberg and Nokihara do not cure the deficiencies of Blanchard. The assertion is noted, however as discussed above, Blanchard is not deemed deficient.

17. Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blanchard (WO 98/41531, published 24 September 1998) in view of Goldberg et al (5,959,098, issued 28 September 1999) and Nokihara (U.S. Patent No. 5,362,447, issued 8 November 1994) as applied to Claim 44 above and further in view of Hillman et al (U.S. Patent No. 4,856,456, issued 15 August 1989).

Regarding Claim 45, Blanchard discloses an apparatus for biopolymer array synthesis (Fig. 5), wherein the apparatus comprise a holding element comprising a grasping element (grooved vacuum chuck, page 61, lines 21-32 and page 66, line 25-page 67, line 8) but is silent regarding finger-like projections on the vacuum chuck. However, vacuum chucks having finger-like projections were well known in the art of substrate processing as taught by Hillman et al.

Hillman teaches a device for treating a substrate surface wherein the substrate is positioned using a vacuum chuck (#104) having fingers (#152) wherein the fingers enhance the sealing between the substrate and vacuum chuck (Column 9, lines 1-9). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the vacuum chuck of Blanchard by adding the fingers of Hillman. One of ordinary skill in the art would have been motivated to do so for the expected benefit of improved sealing of substrate as taught by Hillman (Column 9, lines 1-9).

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### Response to Argument

18. Applicant asserts that Goldberg, Nokihara and Hillman do not cure the deficiencies of Blanchard. The assertion is noted, however as discussed above, Blanchard is not deemed deficient.

### Double Patenting

19. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

20. Claims 30-31, 33-34, 39 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 23-28 of copending Application No. 10/172,470 in view of Blanchard (WO 98/41531, published 24 September 1998). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to flow cell devices comprising a flow cell housing a substrate, fluid dispensing manifold, stations for reagent delivery and mechanical means for moving the support. The claim sets merely differ in that the '470 claims are further drawn to a vacuum source. However, the instant claim language "comprising" encompasses the additional element of the '470 claims. The claim sets further differ in that the instant claims define a computer program for programmed transport of the substrate. Blanchard

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teaches programmed substrate transport whereby methods of oligomer synthesis are fully automated as preferred in the art (page 56, lines 4-9). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the programmed substrate movement of Blanchard to the '470 apparatus. One of ordinary skill in the art would have been motivated to do so for the expected benefit of obtaining fully automated oligomer synthesis as preferred in the art (Blanchard, page 56, lines 4-9).

This is a provisional obviousness-type double patenting

### **Response to Arguments**

21. Applicant asserts that the claim sets differ, at least in the instantly claimed programmed substrate movement. The argument has been considered, but is not found persuasive to overcome the rejection based on the preference for fully automated synthesis apparatus as taught by Blanchard and cited above. rejection because the conflicting claims have not in fact been patented.

22. Claims 30, 32-39, 44-49 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 6,846454 in view of Blanchard (WO 98/41531, published 24 September 1998). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to an apparatus for conducting chemical synthesis, the apparatus comprising a flow cell, fluid dispensing means, a manifold, a mechanism for moving a support and a controller for movement of the mechanism. The claim sets merely differ in the arrangement of limitations within the claims e.g. the movement mechanism and controller are recited in dependent embodiments of the patent claims. The claim sets further differ in that the instant claims define the apparatus as having a plurality of flow cells while the patent claims define a "chamber". However, the patent defines the preferred embodiment of the chamber as having

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multiple flow cells (312a-321e, Column 14, lines 50-66). Therefore, the instantly claimed flow cells are an obvious embodiment of the patent chamber.

The claim sets further differ in that the instant claims define a computer program for programmed transport of the substrate. Blanchard teaches programmed substrate transport whereby methods of oligomer synthesis are fully automated as preferred in the art (page 56, lines 4-9). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the programmed substrate movement of Blanchard to the patent apparatus. One of ordinary skill in the art would have been motivated to do so for the expected benefit of obtaining fully automated oligomer synthesis as preferred in the art (Blanchard, page 56, lines 4-9).

23. Claims 30, 32-39, 44-49 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-33 of U.S. Patent No. 6,713,023 in view of Blanchard (WO 98/41531, published 24 September 1998).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to an apparatus for conducting chemical synthesis, the apparatus comprising a flow cell, fluid dispensing means, a manifold, a mechanism for moving a support and a controller for movement of the mechanism. The claim sets merely differ in the arrangement of limitations within the claims. The claim sets further differ in that the patent claims further define a sealing member. However, the open claim language "comprising" recited in the instant claims encompasses the additional elements of the patent apparatus. Therefore, the instantly claimed flow cells are an obvious embodiment of the patent chamber. The claim sets further differ in that the instant claims define a computer program for programmed transport of the substrate. Blanchard teaches programmed

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substrate transport whereby methods of oligomer synthesis are fully automated as preferred in the art (page 56, lines 4-9). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the programmed substrate movement of Blanchard to the '470 apparatus. One of ordinary skill in the art would have been motivated to do so for the expected benefit of obtaining fully automated oligomer synthesis as preferred in the art (Blanchard, page 56, lines 4-9).

### **Conclusion**

24. No claim is allowed.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

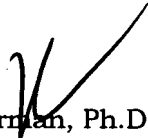
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system

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provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



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